REMARKS

Applicant's attorney wishes to thank the Examiner for the careful consideration given this case. Claims 1, 4, 6-10, and 21-30 are presently pending. This response addresses those issues raised in Office Action dated June 2, 2004. In view of the following remarks, reconsideration of the claims is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

The Examiner rejects Claims 1, 4, 6-10, and 21-30 under 35 U.S.C. § 103(a) as being obvious over Myers et al. (U.S. Patent No. 6,376,472; the '472 patent) in view of Olsson et al. (U.S. Patent No. RE 37,045; the '045 patent). The Examiner asserts that Myers et al. teach a compound of the formula where the ribose ring of the adenosine is a 2',3'-o-isopropylidene derivative. As the Examiner correctly notes, Myers et al. do not provide specific disclosure regarding the substitution of an isopropylidene with an amine group or an alkyl amine group.

The Examiner then cites Olsson et al. for the disclosure where the 5'-carboxamidoadenosine compounds of General Formula 8 (Col. 8 of Olsson et al.) have the substituents of selected from lower alkyl, hydroxyl, lower alkoxy, or halogen substituted straight chain lower alkyl (Col. 7, lines 8-15). However, at no point does the Examiner point to a portion of Olsson et al. that discloses the substitution of an isopropylidene with an amine group or an alkyl amine group, as is claimed in the currently pending claims.

The Examiner's use of Olsson et al. does not cure this deficiency of the '472 patent. The residues R_2 and R_3 of Olsson et al. correspond in part to R_1 and R_2 of the pending claims. The Abstract of Olsson et al. provides a clear definition of R_2

and R_3 as hydrogen or pharmacologically-acceptable acyl groups. The '045 patent expands on this concept at Col. 4, lines 40-49:

> The substituent R_2 and R_3 groups in the compounds of the present invention, as shown in General Formula 3, are hydrogen, or pharmacologically acceptable organic acyl groups, or inorganic acid radicals, such as NO_2 groups, which esterify the hydroxyl groups of the ribofuranose moiety. The R_2 and R_3 groups are preferably of the type which are relatively readily hydrolyzed under physiological conditions. The R_2 and R_3 substituents need not be identical with one another.

It is abundantly clear from this passage and the '045 patent as a whole that Olsson et al. did not contemplate R_2 and R_3 as being amines or alkylamine groups.

Therefore, neither Olsson et al., Myers et al., or their combination discloses or fairly suggests the inventive molecules as claimed in the presently presented claims. As the Examiner is aware, to establish a *prima facie* case of obviousness of a claimed invention, all of the claim limitations must be taught or suggested in the cited references. MPEP § 2143.01. It is submitted that the cited references do not satisfy this requirement in the claims as presently amended. Moreover, the lack of this motif is significant with respect to the functionality of the molecules as described fully in the originally-filed application and detailed hereinbelow. Reconsideration and withdrawal of this rejection are respectfully requested.

Response to Examiner's comments

The present application recognized that numerous anti-hypertensive agents, while reducing blood pressure, also simultaneously cause a marked tachycardia due to reflex activation of the sympathetic nervous system (*See* Paragraph 2). Tachycardia increases myocardial oxygen demand and thus may

worsen myocardial ischemia. To address this problem, the inventors designed the present adenosine receptor agonists to act as rapid-onset/-offset vasodilators that increase blood flow to the brain, heart, gut, and kidneys without causing reflex tachycardia. The inventors specifically inserted a ganglionic blocking motif into the adenosine molecule. This allowed the specific activation of A_{2A} receptors while also blocking the activity of the autonomic nervous system that is responsible for the tachycardia (*See* Paragraph 41). The data presented in Figures 3-6 clearly support this assertion. The ability of a single molecule to reduce blood pressure, while not affecting heart rate, was unknown prior the present invention.

The Examiner asserted on Page 5 of the present Office Action that the "Applicant has not demonstrated any criticality or unexpected result, which stems from the selection of the limitation where R_1 and R_2 are an amine group or an alkyl amine group (substitution on the 2',3'-o-isopropylidene group)." It is respectfully submitted that the inclusion of this sympathetic blocking motif clearly confers just such a criticality and unexpected result, namely the ability to reduce blood pressure without affecting heart rate. Reconsideration and withdrawal of the present rejection is respectfully requested.

In view of the remarks presented herein, it is respectfully submitted that the present application is in condition for final allowance and notice to such effect is requested. If the Examiner believes that additional issues need to be resolved before this application can be passed to issue, the undersigned invites the Examiner to contact him at the telephone number provided below.

Respectfully submitted,

Dated: August 2, 2004

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